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EXAMINER	
TSAY, MARSHA M	
ART UNIT	**PAPER NUMBER**
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,742	HERBERT, BENJAMIN ROSS	
	Examiner	Art Unit	
	Marsha M. Tsay	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19 and 24-51* is/are pending in the application.

4a) Of the above claim(s) *1-18 and 24-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19 and 27-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12.15.08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election with traverse of the species: sonicating the sample; citric acid; thiourea; C7BO; TBP; acrylamide; ammonium sulfate; acetone; amino acid solution, in the reply filed on January 9, 2009, is acknowledged. The traversal is on the ground(s) that a restriction is not proper if claims can be examined together without a serious burden on the PTO (MPEP 803). The reasons are as noted in Applicants' remarks. This is not found persuasive because search of each species would require undue burden due to the fact that each technique is different or each compound is structurally different. However, Applicants request to withdraw at least the species requirement of chaotropic agent (claim 31) is persuasive and therefore, the species requirement of claim 31 is withdrawn.

The requirement is still deemed proper and is therefore made FINAL.

Applicants' arguments, filed February 15, 2008, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

Claims 20-23 are canceled. Claims 1-18, 24-26 are withdrawn. Claims 19, 27-51 are currently under examination.

Priority: The request for priority to AUSTRALIA 2002952533, filed November 4, 2002, is acknowledged.

Objections and Rejections

Claims 33 and 50 are objected to because of the following informalities: in claims 33 and 50, the term "amminio" needs to be corrected to "ammonio"; .

Appropriate correction is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 36 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "substantial" in claim 36 is a relative term which renders the claim indefinite. The term "substantial" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is also unclear how the solubilizing occurs without substantial acid-induced hydrolysis if both the steps in claim 19(i) and 19(ii) recite an acidic pH range. Further clarification is requested.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19, 29, 32, 36, 47-49, 51 are rejected under 35 U.S.C. 102(b) as being anticipated by Sato et al. (1977 European Journal of Biochemistry 78: 557-567; IDS, also previously cited). Sato et al. teach a method of solubilizing membrane fractions by suspending said membrane fractions in lysis buffer containing 8M urea, 2% Triton X-100, 2% ampholines, and 2%

mercaptoethanol at pH 4-6.5 (p. 559; claims 19, 29, 32, 36, 47-49, 51). The "disrupting" limitation that is recited in claims 19(ii) and 48(ii) is believed to be inherently present in the method of Sato et al. since Sato et al. teaches a pH 1.0-6.0. The term "disrupting" has been given its broadest and most reasonable interpretation; therefore, an acidic pH is believed to cause "disruption" of a biological sample.

In their remarks received February 15, 2008, Applicants assert that Sato et al. do not teach all elements of the present claims. Sato et al. do not teach at least the elements of a pH between pH 1.0 and pH 6.0. To the contrary, Sato et al. teach incubating cells with lysozyme "dissolved in 0.1M EDTA (pH 7.5)" and washing cells "in 30mM Tris-HCl (pH 8.1), and suspending in 0.2mL of the same buffer containing 20% w/v sucrose." Applicant's arguments have been fully considered but they are not persuasive.

Applicants are directed to page 559 of Sato et al., which teaches that membrane fractions are solubilized by suspending said membrane fractions in lysis buffer containing 8M urea, 2% Triton X-100, 2% ampholines, and 2% mercaptoethanol at pH 4-6.5. Therefore, Sato et al. is still believed to be a relevant 102(b) reference.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sato et al. (1977 European Journal of Biochemistry 78: 557-567; IDS, also previously cited) in view of knowledge of the art. Sato et al. disclose sonicating the cell membrane fraction but do not disclose sonicating the protein membrane fraction after solubilizing in said lysis buffer.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Sato et al. by disrupting the protein membrane fraction that is incubated in said lysis buffer by sonication in order to enhance the solubilization process (claim 37). The motivation to do so is to break up protein structures that were not previously broken down.

Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sato et al. (1977 European Journal of Biochemistry 78: 557-567; IDS, also previously cited) in view of knowledge of the art (2000 Buffer System Chart). The teachings of Sato et al. are outlined above. Sato et al. do not teach citric acid.

It is known in the art that different types of buffers, including citric acid, can be used to formulate a lysis buffer depending on the protein being solubilized, i.e. citric acid has a pH range of 3.0-6.2 (see buffer system chart).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Sato et al. by using citric acid in the lysis buffer system of Sato et al. (claim 30). The motivation to do is given by general knowledge in the art; it would be reasonable for one of ordinary skill to know that the lysis buffer system of Sato et al. can

incorporate citric acid and still successfully solubilize protein since the pH range of said citric acid is within the acidic pH range taught by Sato et al.

Claims 31, 33-34, 35, 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sato et al. (1977 European Journal of Biochemistry 78: 557-567; IDS, also previously cited) in view of Herbert et al. (US 20040195095). The teachings of Sato et al. are outlined above. Sato et al. do not teach thiourea and tri-n-butylphosphine (TBP).

Herbert et al. teach a solution that solubilizes membrane proteins is a hydrophobic solution comprising 7M urea, 2M thiourea, 1% ASB-14, and 2mM TBP (p. 1 [0008], [0066]).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Sato et al. by adding the thiourea of Herbert et al. and substituting the TBP of Herbert et al. for the mercaptoethanol used in Sato et al. (claims 31, 34). The motivation to do so is given by Herbert et al. which teach that thiourea and TBP are components that can be used in a solution to solubilize membrane proteins; therefore, one of ordinary skill would expect to be successful in adding thiourea (which would enhance the chaotropic properties of the solution) and substituting TBP for mercaptoethanol since both TBP and mercaptoethanol are reducing agents and would have the same functional properties.

Sato et al. do not teach C7BzO.

Herbert et al. teach a hydrophobic solvent used to solubilize membrane proteins can comprise detergents, i.e. Triton X-100, C7BzO (p. 4 [0061]).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Sato et al. by substituting the C7BzO of Herbert et al. for

the Triton X-100 used in Herbert et al. (claims 33, 50). The motivation to do so is given by Herbert et al., which teach C7BzO has the same properties as Triton X-100 in a solution for solubilizing proteins; therefore, one of ordinary skill would expect to be successful in substituting C7BzO for Triton X-100 since both are functionally equivalent.

Sato et al. do not teach an alkylating agent (i.e. acrylamide).

Herbert et al. teach adding an alkylating agent (i.e. acrylamide) to a method of solubilizing a protein (p. 3 [0057]).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Sato et al. by adding the acrylamide of Herbert et al. to the lysis buffer of Sato et al. (claim 35). The motivation to do so is given by Herbert et al., which teach that acrylamide is an alkylating agent that can enhance the solubilization of a protein sample.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 37-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sato et al. (1977 European Journal of Biochemistry 78: 557-567; IDS, also previously cited) in view of Herbert et al. in view of Ryan et al. (US 20030211941). The teachings of Sato et al. in view of Herbert et al. are outlined above. Sato et al. disclose that a solubilized protein fraction can be

precipitated (p. 559 col. 1). Sato et al. or Herbert et al. do not teach precipitation by ammonium sulfate.

Ryan et al. teach that neutral or slightly acidic salts can solubilize or precipitate proteins. Ammonium sulfate is the precipitant used most frequently in the salting out proteins (p. 3 [0032]).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Sato et al. by adding the ammonium sulfate of Ryan et al. after the solubilization step of Sato et al. (claims 37-44). The motivation to do is given by Ryan et al., which teach that ammonium sulfate can be added to solubilize or precipitate a protein; therefore, it would be reasonable for one of ordinary skill to recognize that the addition of ammonium sulfate can help to extract or isolate a desired protein.

Claims 39-44 are included in this rejection because the precipitate would still be suspended in the amino acid solution (thiourea/urea) of Sato et al. It would be reasonable for one of ordinary skill to recognize that the pH of said solution can be adjusted accordingly in order to create the optimum solubilization and precipitation conditions.

Regarding the species recited in claims 45-46, the TBP and acrylamide is taught by Herbert et al. and applied in the same manner as noted in the earlier 103(a) rejection above.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is (571)272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Maryam Monshipouri/

Primary Examiner, Art Unit 1656

March 6, 2009